

WE CLAIM:

1. An injectable depot composition comprising:
 - (a) a low molecular weight bioerodible, biocompatible polymer;
 - (b) a solvent having miscibility in water of less than or equal to 7% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith, wherein said solvent is an aromatic alcohol; and
 - (c) a beneficial agent.
2. An injectable depot composition comprising:
 - (a) a low molecular weight bioerodible, biocompatible polymer;
 - (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and
 - (c) a beneficial agent.
3. The injectable depot composition of claim 1 or claim 2, wherein the aromatic alcohol has the structural formula (I)
$$\text{Ar-(L)}_n\text{-OH}$$
wherein Ar is aryl or heteroaryl, n is zero or 1, and L is a linking moiety.
4. The injectable depot composition of claim 3, wherein Ar is monocyclic aryl or heteroaryl, n is 1, and L is lower alkylene optionally containing at least one heteroatom.
5. The injectable depot composition of claim 4, wherein Ar is monocyclic aryl and L is lower alkylene.
6. The injectable depot composition of claim 5, wherein Ar is phenyl and L is methylene.

7. The injectable depot composition of claim 2, wherein the solvent is mixture of an aromatic alcohol and an ester of an aromatic acid.

8. The injectable depot composition of claim 7, wherein the aromatic alcohol is benzyl alcohol and the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of benzoic acid.

9. The injectable depot composition of claim 8, wherein the ester of an aromatic acid is benzyl benzoate and the lower alkyl ester of an aromatic acid is ethyl benzoate.

10. The injectable depot composition of claim 1 or claim 2 wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 10,000.

11. The injectable depot composition of claim 10, wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 8,000.

12. The injectable depot composition of claim 10, wherein the low molecular weight polymer has a molecular weight ranging from about 4000 to about 6,000.

13. The injectable depot composition of claim 10, wherein the low molecular weight polymer has a molecular weight of about 5000.

14. The injectable depot composition of claim 1 or claim 2, wherein the polymer is selected from the group consisting of polylactides, polyglycolides, polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates,

polyphosphoesters, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, hylauronic acid and copolymers, terpolymers and mixtures thereof.

15. The injectable depot composition of claim 1 or claim 2, wherein the polymer is a lactic acid-based polymer.

16. The injectable depot composition of claim 15, wherein the polymer is a copolymer of lactic acid and glycolic acid.

17. The injectable depot composition of claim 15 comprising about 5 wt.% to about 90 wt.% of a biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of about 3,000 to about 10,000.

18. The injectable depot composition of claim 17, wherein the polymer represents about 10 wt.% to about 85 wt.% of the composition.

19. The injectable depot composition of claim 18, wherein the polymer represents about 35 wt.% to about 65 wt.% of the composition.

20. The injectable depot composition of claim 1 or claim 2, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

21. The injectable depot composition of claim 1 or claim 2 wherein the beneficial agent is selected from a drug, proteins, enzymes, hormones, polynucleotides, nucleoproteins, polysaccharides, glycoproteins, lipoproteins, polypeptides, steroids, analgesics, local anesthetics, antibiotic agents, chemotherapeutic agents, immunosuppressive agents, anti-inflammatory

agents, antiproliferative agents, antimitotic agents, angiogenic agents, antipsychotic agents, central nervous system (CNS) agents, anticoagulants, fibrinolytic agents, growth factors, antibodies, ocular drugs, and metabolites, analogs, derivatives, and fragments thereof.

22. The injectable depot composition of claim 21 wherein the beneficial agent is selected from analgesics, local anesthetics, antibiotic agents, anti-inflammatory agents, antipsychotic agents, anticoagulants, and metabolites, analogs, derivatives, and fragments thereof.

23. The injectable depot composition of claim 21 wherein the beneficial agent is present in an amount of from 0.1 to 50% by weight of the combined amounts of the polymer, the solvent and the beneficial agent.

24. The injectable depot composition of claim 21 wherein the beneficial agent is in the form of particles dispersed or dissolved in the viscous gel.

25. The injectable depot composition of claim 24 wherein the beneficial agent is in the form of particles having an average particle size of from 0.1 to 250 microns.

26. The injectable depot composition of claim 24 wherein the beneficial agent is in the form of particles wherein the particle further comprises a component selected from the group consisting of a stabilizing agent, bulking agent, chelating agent and a buffering agent.

27. An injectable depot composition comprising:

(a) approximately 5 wt.% to approximately 90 wt.% of a low molecular weight bioerodible, biocompatible polymer;

(b) an aromatic alcohol having miscibility in water of less than or equal to 7% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith, wherein the aromatic alcohol has the structural formula (I)



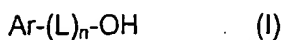
in which Ar is a substituted or unsubstituted aryl or heteroaryl group, n is zero or 1, and L is a linking moiety; and

(c) a beneficial agent.

28. A injectable depot composition comprising:

(a) approximately 5 wt.% to approximately 90 wt.% of a low molecular weight biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of approximately 1,000 to approximately 10,000;

(b) an aromatic alcohol having miscibility in water of less than or equal to 7% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith, wherein the aromatic alcohol has the structural formula (I)



in which Ar is a substituted or unsubstituted aryl or heteroaryl group, n is zero or 1, and L is a linking moiety; and

(c) a beneficial agent.

29. A injectable depot composition comprising:

(a) approximately 5 wt.% to approximately 90 wt.% of a low molecular weight biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of approximately 1,000 to approximately 10,000;

(b) a solvent selected from the group consisting of an aromatic alcohol, an ester of an aromatic acid, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith, wherein the aromatic alcohol has the structural formula (I)



in which Ar is a substituted or unsubstituted aryl or heteroaryl group, n is zero or 1, and L is a linking moiety; and

(c) a beneficial agent.

30. The injectable depot composition of any one of claims 27, 28 or 29 wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 10,000.

31. The injectable depot composition of claim 30, wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 8,000.

32. The injectable depot composition of claim 30, wherein the low molecular weight polymer has a molecular weight ranging from about 4000 to about 6,000.

33. The injectable depot composition of claim 30, wherein the low molecular weight polymer has a molecular weight of about 5000.

34. The injectable depot composition of any one of claims 27, 28 or 29, wherein the polymer is selected from the group consisting of polylactides, polyglycolides, polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, hylauronic acid and copolymers, terpolymers and mixtures thereof.

35. The injectable depot composition of claim 34, wherein the polymer is a lactic acid-based polymer.

36. The injectable depot composition of claim 35, wherein the polymer is a copolymer of lactic acid and glycolic acid.

37. The injectable depot composition of claim 34 comprising about 5 wt.% to about 90 wt.% of a biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of about 3,000 to about 10,000.

38. The injectable depot composition of claim 37, wherein the polymer represents about 10 wt.% to about 85 wt.% of the composition.

39. The injectable depot composition of claim 38, wherein the polymer represents about 35 wt.% to about 65 wt.% of the composition.

40. The injectable depot composition of any one of any one of claims 27, 28 or 29, wherein Ar is monocyclic aryl or heteroaryl, n is 1, and L is lower alkylene optionally containing at least one heteroatom.

41. The injectable depot composition of claim 40, wherein Ar is monocyclic aryl and L is lower alkylene.

42. The injectable depot composition of claim 40, wherein Ar is phenyl and L is methylene.

43. The injectable depot composition of any one of claims 27, 28 or 29, wherein the aromatic alcohol is benzyl alcohol.

44. The injectable depot composition of claim 29, wherein the solvent is mixture of an aromatic alcohol and an ester of an aromatic acid.

45. The injectable depot composition of claim 44, wherein the aromatic alcohol is benzyl alcohol and the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of benzoic acid.

46. The injectable depot composition of claim 45, wherein the ester of an aromatic acid is benzyl benzoate and the lower alkyl ester of an aromatic acid is ethyl benzoate.

47. The injectable depot composition of claim 44, wherein the ratio of the aromatic alcohol to the ester of an aromatic acid is in the range of about 1% to about 99% by weight.

48. The injectable depot composition of claim 47, wherein the ratio of the aromatic alcohol to the ester of an aromatic acid is in the range of about 20% to about 80% by weight.

49. The injectable depot composition of claim 45 comprising about 5 wt.% to about 90 wt.% of a biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of about 3,000 to about 10,000.

50. The injectable depot composition of any one of claims 27, 28 or 29, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

51. The injectable depot composition of any one of claim 27, 28 or 29 wherein the beneficial agent is selected from a drug, proteins, enzymes, hormones, polynucleotides, nucleoproteins, polysaccharides, glycoproteins, lipoproteins, polypeptides, steroids, analgesics, local anesthetics, antibiotic agents, chemotherapeutic agents, immunosuppressive agents, anti-inflammatory agents, antiproliferative agents, antimitotic agents, angiogenic

agents, antipsychotic agents, central nervous system (CNS) agents, anticoagulants, fibrinolytic agents, growth factors, antibodies, ocular drugs, and metabolites, analogs, derivatives, and fragments thereof.

52. The injectable depot composition of claim 51 wherein the beneficial agent is selected from analgesics, local anesthetics, antibiotic agents, anti-inflammatory agents, antipsychotic agents, anticoagulants, and metabolites, analogs, derivatives, and fragments thereof.

53. The injectable depot composition of claim 51 wherein the beneficial agent is present in an amount of from 0.1 to 50% by weight of the combined amounts of the polymer, the solvent and the beneficial agent.

54. The injectable depot composition of claim 51 wherein the beneficial agent is in the form of particles dispersed or dissolved in the viscous gel.

55. The injectable depot composition of claim 54 wherein the beneficial agent is in the form of particles having an average particle size of from 0.1 to 250 microns.

56. The injectable depot composition of claim 54 wherein the beneficial agent is in the form of particles wherein the particle further comprises a component selected from the group consisting of a stabilizing agent, bulking agent, chelating agent and a buffering agent.

57. An injectable depot composition comprising:

(a) approximately 5 wt.% to approximately 90 wt.% a low molecular weight poly(lactide-co-glycolide) (PLGA) copolymer having a weight average molecular weight in the range of approximately 3,000 to approximately 10,000;

- (b) approximately 5 wt.% to approximately 90 wt.% an aromatic alcohol solvent having miscibility in water of less than or equal to 7% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith; and
- (c) a beneficial agent.

58. The injectable depot composition of claim 57, wherein the aromatic alcohol is benzyl alcohol.

59. An injectable depot composition comprising:

(a) approximately 5 wt.% to approximately 90 wt.% of a low molecular weight poly(lactide-co-glycolide) (PLGA) copolymer having a weight average molecular weight in the range of approximately 3,000 to approximately 10,000;

(b) approximately 5 wt.% to approximately 90 wt.% of a solvent selected from the group consisting of an aromatic alcohol, an ester of an aromatic acid, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and

(c) a beneficial agent.

60. The injectable depot composition of claim 59, wherein the aromatic alcohol is benzyl alcohol and the ester of an aromatic acid is benzyl benzoate.

61. An injectable depot composition for sustained delivery of a beneficial agent to a subject comprising:

(a) a low molecular weight bioerodible, biocompatible polymer;

(b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and

(c) a beneficial agent;

wherein the beneficial agent is delivered systemically in a controlled manner over a duration equal to or less than two weeks.

62. An injectable depot composition for sustained delivery of a beneficial agent to a subject comprising:

(a) a low molecular weight bioerodible, biocompatible polymer;

(b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and

(c) a beneficial agent;

wherein the beneficial agent is delivered locally in a controlled manner over a duration equal to or less than two weeks.

63. The injectable depot composition of claim 61 or claim 62 wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 10,000.

64. The injectable depot composition of claim 63, wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 8,000.

65. The injectable depot composition of claim 64, wherein the low molecular weight polymer has a molecular weight ranging from about 4000 to about 6,000.

66. The injectable depot composition of claim 65, wherein the low molecular weight polymer has a molecular weight of about 5000.

67. The injectable depot composition of claim 61 or claim 62, wherein the polymer is selected from the group consisting of polylactides, polyglycolides, polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, hyaluronic acid and copolymers, terpolymers and mixtures thereof.

68. The injectable depot composition of claim 67, wherein the polymer is a lactic acid-based polymer.

69. The injectable depot composition of claim 68, wherein the polymer is a copolymer of lactic acid and glycolic acid.

70. The injectable depot composition of claim 68 comprising about 5 wt.% to about 90 wt.% of a biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of about 3,000 to about 10,000.

71. The injectable depot composition of claim 70, wherein the polymer represents about 10 wt.% to about 85 wt.% of the composition.

72. The injectable depot composition of claim 71, wherein the polymer represents about 35 wt.% to about 65 wt.% of the composition.

73. The injectable depot composition of claim 70, wherein the aromatic alcohol is benzyl alcohol and the ester of an aromatic acid is a lower alkyl ester or an aralkyl ester of benzoic acid.

74. The injectable depot composition of claim 73, wherein the ester of an aromatic acid is benzyl benzoate and the lower alkyl ester of an aromatic acid is ethyl benzoate.

75. The injectable depot composition of claim 70, wherein the solvent is mixture of an aromatic alcohol and an ester of an aromatic acid.

76. The injectable depot composition of claim 75, wherein the ratio of the aromatic alcohol to the ester of an aromatic acid is in the range of about 1% to about 99% by weight.

77. The injectable depot composition of claim 76, wherein the ratio of the aromatic alcohol to the ester of an aromatic acid is in the range of about 20% to about 80% by weight.

78. The injectable depot composition of claim 70, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

79. The injectable depot composition of claim 61 or claim 62 wherein the beneficial agent is selected from a drug, proteins, enzymes, hormones, polynucleotides, nucleoproteins, polysaccharides, glycoproteins, lipoproteins, polypeptides, steroids, analgesics, local anesthetics, antibiotic agents, chemotherapeutic agents, immunosuppressive agents, anti-inflammatory agents, antiproliferative agents, antimitotic agents, angiogenic agents, antipsychotic agents, central nervous system (CNS) agents, anticoagulants, fibrinolytic agents, growth factors, antibodies, ocular drugs, and metabolites, analogs, derivatives, and fragments thereof.

80. The injectable depot composition of claim 79 wherein the beneficial agent is selected from analgesics, local anesthetics, antibiotic agents, anti-inflammatory agents, antipsychotic agents, anticoagulants, and metabolites, analogs, derivatives, and fragments thereof.

81. The injectable depot composition of claim 79 wherein the beneficial agent is present in an amount of from 0.1 to 50% by weight of the combined amounts of the polymer, the solvent and the beneficial agent.

82. The injectable depot composition of claim 79 wherein the beneficial agent is in the form of particles dispersed or dissolved in the viscous gel.

83. The injectable depot composition of claim 79 wherein the beneficial agent is in the form of particles having an average particle size of from 0.1 to 250 microns.

84. The injectable depot composition of claim 79 wherein the beneficial agent is in the form of particles wherein the particle further comprises a component selected from the group consisting of a stabilizing agent, bulking agent, chelating agent and a buffering agent.

85. A method of administering a beneficial agent to a subject in a controlled manner over a duration equal to or less than two weeks, comprising administering an injectable depot composition comprising:

- (a) a low molecular weight bioerodible, biocompatible polymer;
- (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and
- (c) a beneficial agent.

86. A method of administering a beneficial agent to a subject comprising administering an injectable depot composition comprising:

- (a) a low molecular weight bioerodible, biocompatible polymer;
- (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and
- (c) a beneficial agent;

wherein the beneficial agent is delivered systemically in a controlled manner over a duration equal to or less than two weeks.

87. A method of locally administering a beneficial agent to a subject in a controlled manner over a duration equal to or less than two weeks, comprising administering an injectable depot composition comprising:

- (a) a low molecular weight bioerodible, biocompatible polymer;
- (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and
- (c) a beneficial agent;

the system releasing within 24 hours after implantation less than or equal to 20% by weight of the amount of beneficial agent to be delivered over the duration of the delivery period, wherein the delivery period is 2 weeks.

88. A method of administering a beneficial agent to a subject comprising administering an injectable depot composition comprising:

- (a) a low molecular weight bioerodible, biocompatible polymer;
- (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent

having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and

(c) a beneficial agent;

wherein the beneficial agent is delivered locally in a controlled manner over a duration equal to or less than two weeks.

89. The method of any one of claims 85, 86, 87 or 88 wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 10,000.

90. The method of claim 89, wherein the low molecular weight polymer has a molecular weight ranging from about 3000 to about 8,000.

91. The method of claim 90, wherein the low molecular weight polymer has a molecular weight ranging from about 4000 to about 6,000.

92. The method of claim 91, wherein the low molecular weight polymer has a molecular weight of about 5000.

93. The method of any one of claims 85, 86, 87 or 88, wherein the polymer is selected from the group consisting of polylactides, polyglycolides, polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, hylauronic acid and copolymers, terpolymers and mixtures thereof.

94. The method of claim 93, wherein the polymer is a lactic acid-based polymer.

95. The method of claim 94, wherein the polymer is a copolymer of lactic acid and glycolic acid.

96. The method of claim 94 comprising about 5 wt.% to about 90 wt.% of a biodegradable, biocompatible lactic acid-based polymer having a weight average molecular weight in the range of about 1,000 to about 5,000.

97. The method of claim 96, wherein the polymer represents about 10 wt.% to about 85 wt.% of the composition.

98. The method of claim 94, further including at least one of the following: a pore former; a solubility modulator for the beneficial agent; and an osmotic agent.

99. The method of any one of claims 85, 86, 87 or 88, wherein the beneficial agent is selected from a drug, proteins, enzymes, hormones, polynucleotides, nucleoproteins, polysaccharides, glycoproteins, lipoproteins, polypeptides, steroids, analgesics, local anesthetics, antibiotic agents, chemotherapeutic agents, immunosuppressive agents, anti-inflammatory agents, antiproliferative agents, antimitotic agents, angiogenic agents, antipsychotic agents, central nervous system (CNS) agents, anticoagulants, fibrinolytic agents, growth factors, antibodies, ocular drugs, and metabolites, analogs, derivatives, and fragments thereof.

100. The method of claim 99 wherein the beneficial agent is selected from analgesics, local anesthetics, antibiotic agents, anti-inflammatory agents, antipsychotic agents, anticoagulants, and metabolites, analogs, derivatives, and fragments thereof.

101. The method of claim 99 wherein the beneficial agent is present in an amount of from 0.1 to 50% by weight of the combined amounts of the

polymer, the solvent and the beneficial agent.

102. The method of claim 99 wherein the beneficial agent is in the form of particles dispersed or dissolved in the viscous gel.

103. The method of claim 99 wherein the beneficial agent is in the form of particles having an average particle size of from 0.1 to 250 microns.

104. The method of claim 99 wherein the beneficial agent is in the form of particles wherein the particle further comprises a component selected from the group consisting of a stabilizing agent, bulking agent, chelating agent and a buffering agent.

105. A kit for administration of a beneficial agent to a subject comprising:

- (a) a low molecular weight bioerodible, biocompatible polymer;
- (b) a solvent selected from the group consisting of aromatic alcohols, esters of aromatic acids, aromatic ketones, and mixtures thereof, said solvent having miscibility in water of less than or equal to 7% at 25°C, and present in an amount effective to plasticize the polymer and form a gel therewith; and
- (c) a beneficial agent; and optionally, one or more of the following:
 - (d) an emulsifying agent;
 - (e) a pore former;
 - (f) a solubility modulator for the beneficial agent, optionally associated with the beneficial agent; and
 - (g) an osmotic agent;

wherein at least the beneficial agent, optionally associated with the solubility modulator, is maintained separated from the solvent until the time of administration of the beneficial agent to a subject.